

## **REMARKS**

### **Amendments to the Claims**

Applicants have amended claims 3-14 and 21, withdrawn claims 1-2, 19, and 27-30 and canceled claims 15-18, 20, and 24-26. Upon entry of these amendments, claims 3-14 and 21-23 remain pending.

Applicants have amended claim 3 to clarify the substituted substituents recited in the claim. Support for this amendment is found throughout the specification. *See e.g.*, paragraphs [0055]-[0068], [0073], [0075], [0080], [0081], [0091], and [0105]-[0108]. Applicants also amended claim 3 to recite the size of the possible heterocycle formed by  $R_1$  and  $R_2$ . Support for this amendment can be found, for example, on page 39, lines 8-10 (paragraph [0091]). Finally, amended claim 3 clarifies what substituents may be encompassed by  $R_3$ . Support for this amendment can be found, for example, in previously filed claim 3 and paragraph [0081] of the specification.

Applicants have amended the other remaining claims to be consistent with amended claim 3.

Applicants have also amended claim 14 to define the nature of the carrier. Support for this amendment can be found, for example, in paragraph [0128].

Finally applicants have amended claim 21. The amendment clarifies to the skilled practitioner how to treat a given subject. Support for this amendment can be found, for example, in paragraphs [0126], [0128]-[0148], and [0150]-[0165]; Example 21; and Example 22 of the specification.

Applicants request entry of these amended claims

Applicants have made these amendments, withdrawn some of the claims, and canceled other of the claims without prejudice. They reserve the right to seek patents on the canceled, amended, or withdrawn subject matter in this or other applications claiming priority or benefit from this application.

### **The Rejections**

#### **1. 35 U.S.C. §112, second paragraph: Indefiniteness**

Claims 3-18 and 20-26 stand rejected as allegedly indefinite. In particular, the Examiner argues that the nature of the prodrug, the nature of substitutions, the nature of heteroaryl, and the term heterocyclic are unclear and indefinite. He also argues that the pharmaceutical composition of claim 14 is indefinite as lacking a carrier. He argues that claims 15-18 are improper as allegedly duplicates of compound claim 3 or pharmaceutical composition claim 15. Finally, he contends that claims 24-26 are improper use claims allegedly reciting a use but not reciting the steps involved in the method/process. In view of the various claim amendments and arguments, applicants traverse these indefiniteness rejections.

##### **(i) Prodrug**

Applicants have amended all of the remaining claims to omit the term "prodrug". This moots the rejection.

(ii) Substituted

Claims 3-14, as amended, are not indefinite. They also find specific definition and support in the Detailed Description of the Invention of the present specification. In particular, the specification describes appropriate substituents to be incorporated in the functional groups recited in the claims (*e.g.*, [0055]-[0068], [0073], [0075], [0080], [0081], [0105]-[0108], and [0118] of the specification). Indeed, examples of many specific substituents are listed in Tables 1 and 2 of the specification.

(iii) "Heteroaryl"/"Heterocyclic"

The application provides specific examples of heterocyclic and heteroaryl groups. They include, for example, furyl, thienyl, and the like (*e.g.*, paragraph [0091]). Claim 3, as amended, clarifies the number of atoms in the intended heterocyclic rings formed by R1 and R2 (*e.g.*, page 39, lines 8-10 ). This overcomes the rejection.

(iv) Carrier

Applicants have amended claim 14 to recite a carrier. This moots the rejection.

(v) Claims 15-18

Applicants have canceled claims 15-18. This moots the rejection.

(vi) Claims 24-26

Applicants have canceled claims 24-26. This moots the rejection.

In view of the above described claim amendments and cancellations and arguments, applicants request that the Examiner reconsider and withdraw all of the indefiniteness rejections.

## **2. 35 U.S.C. §101: Non-statutory subject matter**

Claims 24-26 stand rejected as non-statutory as allegedly reciting a use without steps. Applicants have canceled claims 24-26. This moots the rejection.

## **3. 35 U.S.C. §112, First Paragraph: Enablement**

### **(i) Solvates**

Claims 3-8 and 20-26 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled. In particular, the Examiner argues that, while being enabled for pharmaceutical salts, the specification does not enable the claimed solvates. Applicants traverse.

One skilled in the art would readily understand and would be able to prepare solvates of the claimed compounds routinely and without the exercise of inventive skill. Solvates are described, for example, in paragraph [0124] of the present specification. Specific examples of prepared solvates of claimed compounds are also disclosed in the application (see, *e.g.*, Compounds B198, B199, B218, B245, B249, B277, B314, and B319 on pg 181-208). Further, the preparation of solvates was well known in the art at the filing date of the application. *See e.g.*, M. Caira et al, *J. Pharmaceutical Sci.*, 93(3), 601-11 (2004); E.C. van Tonder et al, *AAPS PharmSciTech.*, 5(1), article 12 (2004); and A.L. Bingham et al, *Chem. Commun.*, 603-4 (2001). For all of these reasons, the skilled worker would easily have been able to make solvates of the claimed compounds with no more than ordinary skill. Applicants request reconsideration and withdrawal of this rejection.

(ii) Treating/Preventing NAD(P)H Diseases

Claim 21 stands rejected as allegedly not enabled. The Examiner contends that the specification does not teach the skilled worker how to use the claimed method of treating or preventing NAD(P)H-related diseases. In particular, the Examiner argues that the application has not taught what is being treated, who the patient is, how the patient can be identified, the dose to be used, the dosage regimen, the route of administration, and what disease or symptoms is being treated. Applicants traverse.

Claim 21, as amended, clarifies the claimed method of treatment or prevention.

Given the metes and bounds of amended claim 21, one skilled in the art would be able to readily perform the claimed method by administering an amount of the claimed compounds that is effective to inhibit NAD(P)H oxidase without inventive skill.. Indeed, the application provides specific examples of doing just that. In particular, Example 21 describes the *in vitro* inhibition of NAD(P)H oxidase by compounds of the present invention. Example 22, on the other hand, demonstrates the *in vivo* inhibition of NAD(P)H oxidase in neutrophils, blood vessels and circulatory diseases, and gastric mucosa disorders. Moreover, paragraphs [0128]-[0148], for example, describe how one skilled in the art would prepare the claimed compounds into pharmaceutical compositions (*e.g.*, tablet, pill or liquid preparation). Finally, paragraphs [0126] and [0150]-[0164], for example, describe routes of administration, various delivery systems, and diseases known to be related to NAD(P)H. Additionally, the specification describes a range of appropriate dosages (*e.g.*, paragraph [0165]).

In view of these disclosures and actual examples, one skilled in the art would readily understand, prepare, and be able to administer a therapeutically effective amount of the claimed compounds, and solvates thereof, to inhibit NAD(P)H oxidase in methods for treating NAD(P)H oxidase-related diseases. Applicants request reconsideration.

#### **4. 35 U.S.C. §102: Anticipation**

##### **(i) Elworthy**

Claims 3, 4, 6, 7, and 20 stand rejected as allegedly anticipated by Elworthy et al., *Journal of Medicinal Chemistry*, (1997), 40(17), 2674-87 ("*Elworthy*"). On page 7 of the Office Action, the Examiner relies on a chemical structure, wherein moieties R1 and R2 are alkyls, moiety R3 is a mono-lower alkyl amino group, moiety R4 is hydrogen, and moiety R5 is a halogen. Applicants traverse to the extent the anticipation rejection is mentioned in view of the amended claim.

Applicants have amended claim 3 (and thus dependent claims 4, 6, and 7) and canceled claim 20. As amended, claim 3, the sole independent claim, no longer recites that R3 includes "mono-lower alkyl amino." As such, *Elworthy* no longer anticipates the compounds of the amended claims.

##### **(ii) Kiyokawa**

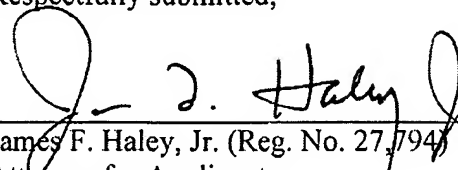
Claim 20 stands rejected as allegedly anticipated by Kiyokawa et al. (US 5,420, 128) ("*Kiyokawa*"). Applicants have canceled claim 20. This moots the rejection.

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**CONCLUSION**

Applicants request favorable consideration and early allowance of the amended claims.

Respectfully submitted,



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